**UNITED STATES DISTRICT COURT**
**FOR THE**
**DISTRICT OF MASSACHUSETTS**

02 CV 11280 RWZ

**ARIAD PHARMACEUTICALS, INC., MASSACHUSETTS INSTITUTE OF TECHNOLOGY, THE WHITEHEAD INSTITUTE FOR BIOMEDICAL RESEARCH, and THE PRESIDENT AND FELLOWS OF HARVARD COLLEGE**

**Plaintiffs,**

**v.**

**ELI LILLY & CO.,**

**Defendant.**

**No.** _____

**Jury Trial Demanded**



**COMPLAINT**

Plaintiffs ARIAD Pharmaceuticals, Inc. ("ARIAD"), Massachusetts Institute of Technology ("M.I.T."), the Whitehead Institute for Biomedical Research ("THE WHITEHEAD INSTITUTE"), and the President and Fellows of Harvard College ("HARVARD") (hereinafter collectively referred to as "Plaintiffs"), through their attorneys, for their Complaint against Defendant Eli Lilly & Co. ("Lilly"), allege as follows:

## NATURE OF THE ACTION

1. This is a patent infringement action against Lilly based on Lilly's activity in connection with its Xigris® and Evista® products covered by claims of Plaintiffs' United States Patent No. 6,410,516 ("the '516 patent"), entitled "Nuclear Factors Associated With Transcriptional Regulation." A copy of the patent is attached as Exhibit 1.

2. Plaintiffs seek monetary damages, including but not limited to a reasonable royalty for Defendant Lilly's current and future infringement of the '516 patent.

## PARTIES, JURISDICTION AND VENUE

3. ARIAD is a corporation organized and existing under the laws of the State of Delaware with its principal place of business located at 26 Landsdowne Street, Cambridge, Massachusetts.

4. M.I.T is a co-educational, privately endowed research university located at 77 Massachusetts Avenue, Cambridge, Massachusetts.

5. THE WHITEHEAD INSTITUTE is a non-profit research and education institute located at Nine Cambridge Center, Cambridge, Massachusetts. It is affiliated with M.I.T in its teaching activities, but is wholly responsible for its own research programs, governance, and finance.

6. HARVARD is a co-educational, privately endowed research university located at Massachusetts Hall, Cambridge, Massachusetts.

7. Upon information and belief, Defendant Lilly is a corporation organized and existing under the laws of the State of Indiana with its principal place of business located at Lilly Corporate Center, Indianapolis, Indiana. Lilly does substantial business in this judicial district.

8. This is an action for patent infringement under the Patent Act of the United States, 35 U.S.C. § 100 *et seq.*, including §§ 271 and 281. This Court has subject matter jurisdiction over this patent infringement action pursuant to 28 U.S.C. § 1338(a).

9. Venue is proper in this judicial district pursuant to §§ 1400(b) and 1391(c).

## FACTUAL BACKGROUND

10. Living cells respond to a vast array of different signals in their environment, including natural regulatory factors (e.g. hormones) and harmful factors (e.g. toxins). A primary way that cells respond to such signals is through intricate networks of signaling proteins inside the cell, which act as "messengers" to regulate expression of genes that are critical for normal cell function. Normal cell signaling and gene regulation are both controlled at a molecular level by specific interactions of these "messenger" proteins with other proteins and DNA. Identifying these "messenger" proteins and how they function is a crucial step in developing drugs for treating diseases associated with abnormal cell signaling and gene regulation.

11. The invention of the '516 patent arose from a collaboration between research groups at three of the world's leading biomedical research institutions, M.I.T., THE WHITEHEAD INSTITUTE, and HARVARD. The collaboration was directed by three distinguished scientists, Dr. David Baltimore, Nobel Laureate and former director of THE WHITEHEAD INSTITUTE, Dr. Phillip Sharp, also a Nobel Laureate and now Institute Professor at M.I.T., and Dr. Thomas Maniatis, Thomas H. Lee Professor of Molecular and Cellular Biology at HARVARD.

12. In the mid 1980s, Dr. Baltimore and his colleagues identified a "messenger" protein, which they named "NF-KB." As discussed in the '516 patent specification, Dr. Baltimore and his colleagues initially believed that NF-KB was only found in certain cells known as "B cells" and, therefore, had a limited role in cell signaling and gene regulation.

13. Extensive studies on NF-KB carried out by the named inventors in Dr. Baltimore's laboratory at THE WHITEHEAD INSTITUTE and the other co-inventors in Dr. Sharp's laboratory at M.I.T. and Dr. Maniatis' laboratory at HARVARD led to the surprising discovery, described in the '516 patent, that NF-KB is found in "many, if not all, cell types and that it acts as an intracellular messenger capable of playing a broad role in gene regulation as a mediator of inducible signal transduction." ('516 patent col. 2, lines

29-31.) Most significantly, through the work disclosed in the '516 patent, the inventors also showed how the NF-KB cell-signaling pathway could be regulated and used for medical and therapeutic applications.

14. ARIAD, since its founding in 1991, has been engaged in research and development of pharmaceutical products that regulate cell signaling pathways and gene function. ARIAD's drug discovery program is aimed at developing small-molecule drugs to inhibit or block disease-related abnormal cell-signaling and to control gene function and cell-signaling.

15. In part for his preeminent contribution to the cell-signaling field and the relevance of this expertise to ARIAD's research and development program, ARIAD invited, and Dr. Baltimore agreed, to join ARIAD's board of scientific and medical advisors as a founding member.

16. In 1986, the first of a series of U.S. patent applications relating to the NF-KB research spearheaded by Dr. Baltimore and various of his co-inventors was filed. Through extensive prosecution, during which the Patent Office carefully scrutinized the claimed subject matter for compliance with the statutory requirements for patentability, the Patent Office awarded the inventors several patents claiming various, separate aspects of this pioneering technology. The '516 patent asserted herein, is the most recent patent to issue of this family of patents.

## THE PATENT-IN-SUIT

17. On June 25, 2002, the '516 patent, entitled "Nuclear Factors Associated With Transcriptional Regulation," with claims that cover methods of treating human disease by regulating NF-KB activity, was duly and legally issued to Baltimore *et al.* and assigned to M.I.T. THE WHITEHEAD INSTITUTE, and HARVARD.

18. Based on a license agreement executed in 1991, ARIAD is the exclusive licensee from M.I.T., THE WHITEHEAD INSTITUTE, and HARVARD of the '516 patent, which presents claims directed to

one aspect of the pioneering technology discovered by the inventors, i.e., the use of drugs that regulate NF-KB cell signaling.

## LILLY'S INFRINGEMENT OF THE '516 PATENT

19. Upon information and belief, Lilly is engaged in the manufacture, importation, use, sale and/or offers of sale, and promotion of pharmaceutical products marketed under the brandname Evista®.

20. Upon information and belief, Evista® is a form of the selective estrogen receptor modulator raloxifene hydrochloride, and was approved for sale by the United States Food and Drug Administration on or about December 10, 1997, for the prevention and treatment of osteoporosis in postmenopausal women.

21. Upon information and belief, a molecular basis for the action of Evista® in treating osteoporosis has been demonstrated to occur through the modulation of NF-KB activity. Some of these findings were published by Lilly scientists in a World Intellectual Property Organization Patent Application entitled "Methods of Modulating NF-KB Transcription Factor" and bearing publication number WO 96/40137. A copy of this patent application is attached as Exhibit 2.

22. Upon information and belief Lilly is engaged in the manufacture, importation, use, sale and/or offers of sale and promotion of pharmaceutical products marketed under the brandname Xigris®.

23. Upon information and belief, Xigris® is a form of recombinant human activated protein C, and was approved for sale by the United States Food and Drug Administration on or about November 21, 2001, for the reduction of mortality in human adult patients with severe sepsis who have a high risk of death.

24. Upon information and belief, a molecular basis for the action of Xigris® in treating septic shock has been demonstrated to occur through the inhibition of NF-KB activity. These findings were published

by Lilly scientists in papers by Joyce *et al.*, J. Biol. Chem., 276: 11199-11203, 2001 and Crit. Care Med. 30:S288-S293, 2002. Copies of these papers are attached as Exhibits 3 and 4.

25. Plaintiffs have suffered and will continue to suffer damages as a result of Lilly's infringing activities.

26. Plaintiffs have previously sought to initiate discussions with Lilly concerning a license to Plaintiffs' NF-KB patent estate. Defendant Lilly has failed to respond to these efforts.

## COUNTS

### Count 1 – Patent Infringement of the '516 Patent

27. Paragraphs 1-26 of this Complaint are incorporated by reference as if stated fully herein.

28. Defendant Lilly, by engaging in the unauthorized manufacture, importation, use, sale and/or offers for sale of raloxifene hydrochloride in the United States, including pharmaceutical products marketed as Evista®, has committed acts of direct, contributory and/or induced infringement of claims 69-72, 80, 82, 84, 85 and 93-96 of the '516 patent.

29. Defendant Lilly, by engaging in the unauthorized manufacture, importation, use, sale and/or offers for sale of recombinant human activated protein C in the United States, including pharmaceutical products marketed as Xigris®, has committed acts of direct, contributory and/or induced infringement of claims 14, 15, 144-146, and 154-156 of the '516 patent.

30. Defendant Lilly has offered for sale, sold and/or imported raloxifene hydrochloride into the United States, including pharmaceutical products marketed as Evista®, with knowledge that such products have a molecular basis of action through the modulation of NF-KB activity and are especially made or adapted for use in an infringment of the '516 patent. Evista®, which constitutes a material part of the invention, is not a staple article or commodity of commerce suitable for substantial non-infringing

use. By its actions, Defendant Lilly is actively and knowingly inducing infringement of claims 69-72, 80, 82, 84, 85 and 93-96 of the '516 patent.

31. Defendant Lilly has offered for sale, sold and/or imported recombinant human activated protein C into the United States, including pharmaceutical products marketed as Xigris®, with knowledge that such products have a molecular basis of action through the inhibition of NF-KB activity and are especially made or adapted for use in an infringement of the '516 patent. Xigris® which constitutes a material part of the invention, is not a staple article or commodity of commerce suitable for substantial non-infringing use. By its actions, Defendant Lilly is actively and knowingly inducing infringement of claims 14, 15, 144-146, and 154-156 of the '516 patent.

32. Plaintiffs have suffered and will continue to suffer damages as a result of Defendant's infringing activities.

WHEREFORE, Plaintiff respectfully request that the Court:

A. Award to Plaintiffs damages adequate to compensate Plaintiffs for infringement of the '516 patent, but in no event less than a reasonable royalty, together with interest and costs.

B. Enter an order declaring this an exceptional case pursuant to 25 U.S.C. § 285 and award to Plaintiffs reasonable attorney fees;

and,

C. Grant to Plaintiffs such other and further relief as may be just and appropriate.

**JURY DEMAND**

Pursuant to Fed. R. Civ. P. 38, Plaintiffs respectfully demand a trial by jury on all issues that are properly triable to a jury in this action.

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